Rheumatology

Inflammatory arthritis

Seropositive arthritis:
1. Rheumatoid arthritis
2. Systemic lupus erythematosus
3. Scleroderma
4. Sjögren's syndrome
5. Polymyositis-Dermatomyositis
6. Mixed CTD

Seronegative arthritis:
1. Ankylosing spondylitis
2. Psoriatic arthritis
3. Reactive arthritis
4. Enteropathic arthritis

Crystal induced arthropathies:
1. Gout
2. Pseudogout

Vasculitis syndromes
1. Behcet's disease
2. Giant cell arthritis
3. Polymyalgia rheumatica
4. Wagner's granulomatosis

Septic arthritis

Non-Inflammatory arthritis

Osteoarthritis

Fibromyalgia

Introduction to Rheumatology

What are Rheumatic diseases?
They are syndromes of pain and/or inflammation in articular or periarticular tissue.

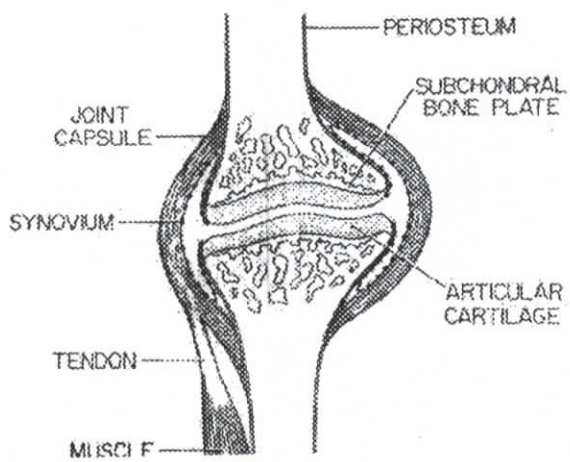
Articular and periarticular structures

Structure of the joint: The synovial joint consists of 2 articular surfaces, enclosed by a fibrous capsule lined with synovium. The space between the articular cartilages is filled with synovial fluid acting as a lubricant.

Periarticular structures (structures surrounding the joints):

- Tendon insertions on bone (**enthuses**)
- Muscles
- Ligaments
- Bursae

- The articular cartilage is covered by avascular hyaline cartilage made of chondrocytes.
- The synovium is a vascular membrane that produces synovial fluid. The synovium has 2 types of cells:
    1. Synovial macrophages which are phagocytic cells.
    2. Synovial fibroblasts which are secretory cells.
- The synovial fluid is derived from plasma and has a high concentration of hyaluronic acid giving high viscosity.
- Joint pain sensation come from the capsule, periosteum and ligaments.



Note: While bone can regenerate if damaged the cartilage cannot regenerate.

Rheumatoid Arthritis

Definition

Rheumatoid arthritis is a chronic immune mediated inflammatory disorder of unknown cause that is characterized by synovial cell proliferation & inflammation leading to destruction of adjacent articular tissue.
The presentation is polyarticular, symmetrical joint involvement ± extra-articular involvement. The disease runs a relapsing remitting course.

Epidemiology

Prevalence: worldwide **1%** . RA is the most common cause of inflammatory arthritis in females.
Age: peak age of onset is early 40s.
Gender: More in Females with F/M ratio **3:1**
Genetic:

- **HLA associations:** HLA-DR4 and it is a marker for severe RA & poor prognosis.
- More in twins

Environment: cigarette smoking is a risk factor.

Etiology & Pathogenesis

Genetic predisposition + Unknown antigen → Immune mediated response → inflammation → Synovial tissue proliferation (Pannus) → destruction of cartilage → subluxation, and mechanical instability of joints.

As any inflammation there are:

- Angiogenesis (Endothelial cell activation)
- Recruitment of inflammatory cells to the joint (lymphocytes, plasma cells, macrophages, and fibroblasts).
- Amplification of inflammation occurs in response to local production of inflammatory cytokines (tumor necrosis factor alpha [**TNF-α**] and interleukin-1 [**IL-1**].

Pathology

- **Pannus** is the characteristic pathological lesion in RA, which is a thickened inflammatory granulation tissue formed of synovial tissue proliferation.
- Pannus is locally invasive and the cells within the Pannus produce destructive collagenases and proteases. These enzymes mediate the erosion of cartilage at the subchondral bone/cartilage junction and inwards until the articular cartilage is destroyed.

Clinical manifestations

Articular manifestations:

- Typically a symmetric polyarthritis of peripheral joints with pain, tenderness, and swelling of affected joints; morning stiffness is common.
- Redness is not a feature of RA and it indicate an infection of the joint.
- Characteristically involves joints are hand joint (PIP, MCP, Wrist) and feet joints metatarsophalangeal (MTP) and knees; joint deformities may develop after persistent inflammation.
- Enthuses are spared unlike seronegative arthropathies
- Baker's cysts: it occur in pt with knee synovitis, with synovial fluid accumulation in the cyst. If ruptured it gives picture like DVT, but here anticoagulants are contraindicated.

Extraarticular manifestations:

Cutaneous—Rheumatoid nodules, vasculitis, palmar erythema, Raynaud's syndrome and pyoderma gangrenosum.

Pulmonary— pleural effusion is the most common pulmonary complication, more in male, nodules, interstitial lung disease, bronchiolitis, Caplan's syndrome [sero(+) RA associated with pneumoconiosis]

Ocular- it is common, with 25% of patients having eye problems.

How the eye becomes involved in RA?

- Keratoconjunctivitis sicca due to secondary Sjögren's syndrome is (**most common ocular manifestation RA pts**).
- Episcleritis (erythema).
- Scleritis (erythema and pain).
- Corneal ulceration.
- Keratitis.
- Scleromalacia.
- Scleromalacia perforans.
- Iatrogenic causes:
    - Steroid-induced cataracts
    - Chloroquine retinopathy

Hematologic: Anemia of chronic illness, Eosinophilia , Generalized lymphadenopathy, Felty's syndrome (splenomegaly and neutropenia).

Cardiac: pericarditis (most common cardiac complication), myocarditis, conduction problems.

Neurologic: Entrapment syndromes e.g. carpal tunnel syndrome. Myelopathies secondary to cervical spine disease. Vasculitis causing mononeuritis multiplex or Peripheral neuropathy with 'glove and stocking' distribution.

Others—Amyloidosis of AA type → Nephrotic syndrome.

What about vascular involvement in RA?

Vasculitis can affect all sizes of vessels:

- Small end-arteries: nail-fold & digital infarcts, gangrene, skin ulceration
- Large arteries (rarely affected): stroke, mesenteric or limb ischemia.
- Medium and Small arteries: mononeuritis multiplex (through involvement of vasa nervorum) and patchy muscle ischemia.
- **The renal vasculature is spared.**

In patient with RA who develops proteinuria how can you explain that?

The kidney in RA may be affected by:

- Amyloidosis resulting in nephrotic syndrome.
- Drugs: gold salts, penicillamine, both can cause nephrotic syndrome.

*What do you about the **rheumatoid nodules**?*

- They are present in about 25% of cases.
- Site: On extensor surface of ulna and over the olecranon, flexor and extensor tendons of the hand, sacrum, Achilles tendon, sclera, lungs, pleura, myocardium, & meninges
- They are usually asymptomatic
- They are one of the criteria for diagnosis of RA
- There presence indicates:
  1- Active disease
  2- RF is being + in 100%
  3- More aggressive disease with extra-articular manifestations

*What is **Felty's syndrome**?*

- Felty's syndrome consists of chronic RA, splenomegaly, neutropenia ± anemia & thrombocytopenia, lymphadenopathy and hepatomegaly
- More in females, and occurs in old age > 50 years.
- Splenectomy ameliorates hypersplenism.
- Felty's syndrome is associated with +ve RF & rheumatoid nodules

What factors have been implicated in anemia of chronic disease?

1- Decreased production of red blood cells
2- Due to inadequate iron: impaired absorption and transport, failure to release iron stores. [**Hepcidin** related]
3- Bone marrow resistance to erythropoietin.
4- Increased destruction of red cells.

What are the Poor prognostic features of RA ?

1. Female sex ♀
2. HLA DR4
3. Insidious onset
4. Extra articular features e.g. **nodules**
5. Poor functional status at presentation
6. Rheumatoid factor positive
7. X-ray: early erosions (e.g. after < 2 years)

Investigations

- **Rheumatoid factor**:
  - Rheumatoid factor (RF) is an IgM antibody which reacts with the Fc portion of the patients IgG.
  - RF is positive in 75% of pts; its presence correlates with severe disease, nodules, & extraarticular features (but NOT a marker of disease activity)
- Other laboratories:
  - CBC:
    - RBC → normocytic normochromic anemia.
    - WBC → Leukocytosis or neutropenia (Felty's syndrome).
    - Platelets →Thrombocytosis or thrombocytopenia (Felty's syndrome).
  - ESR and CRP: both are elevated.
- Synovial fluid analysis—useful to rule out crystalline disease, infection.
- Radiographs—**x-ray changes** include:
  - Early x-ray findings
    - Narrowing of joint space.
    - Periarticular osteopenia.
    - Soft-tissue swelling
  - Late x-ray findings
    - Marginal erosions.
    - Subluxation
- CXR should be obtained.

Monitoring

- Hx: Morning stiffness.
- Ex: Joint tenderness.
- ESR, CRP &hemoglobin levels are used to monitor response to treatment.

Diagnostic criteria for the diagnosis of RA		
	Criterion	**Definition**
1	Morning stiffness	Morning stiffness in & around the joints, lasting at least 1 hour before maximal improvement
2	Arthritis of three or more joints	Soft tissue swelling or fluid (not bony overgrowth alone). 14 possible areas are right or left PIP, MCP, wrist, elbow, knee, ankle, and MTP joints.
3	Arthritis of hand	At least one area swollen in a wrist, MCP, or PIP joint
4	Symmetrical arthritis	Simultaneous involvement of the same joint areas bilaterally (bilateral involvement of PIPs, MCPs, or MTPs is acceptable without absolute symmetry)
5	Rheumatoid nodules	Subcutaneous nodules over bony prominences, or extensor surfaces, or in juxta-articular regions, observed by a physician
6	Serum rheumatoid factor positive	
7	Radiographic changes	Radiographic changes typical of rheumatoid arthritis on hand and wrist radiographs, which must include evidence of erosions or periarticular osteopenia (osteoarthritis changes alone do not qualify)
	A patient is said to have RA if he/she has satisfied at least four of these seven criteria. The first four criteria must have been present for **at least 6 weeks**.	

What are the typical changes of RA in hands?

(1) Hyperextension of PIP joints & flexion of DIP joints **(Swan-neck deformity)**
(2) Flexion of PIP joints and extension of DIP joints **(Boutonnière deformity)**
(3) Thumb: Hyperextension of IP joint and flexion of the first MCP joint **("Z" deformity)**
(4) Ulnar deviation of the digits at the MCP.
(5) Palmar subluxation of the digits at the MCP.
(6) Radial deviation of the metacarpal bones at the wrist
(7) Dorsal sublaxation of the ulna at the wrist**(Piano key deformity of wrist)**

Examination of rheumatoid hands					
Action	YES	NO	**Action**	YES	NO
Permission taken			**Range & Power**		
Stood on the Right side of bed			Wrist		
Adequate Exposure			Abduction		
Ask pt to put hands on the pillow			Adduction with paper test		
Inspection			Thumb to Fingers opposition		
Nails			Hand grip		
Skin (Scar, Palmar erythema)			**Functional assessment**		
Ms (Wasting)			Unbuttoning & buttoning		
Joints (Deformity & Swelling)			Writing		
Palpation			**I would like to**		
Ask if there is any pain			Examine other joints and check for splenomegaly & lower lobe fibrosis		
Hotness					
Tenderness			**Ethics**		
For Area of swelling			Dress the patient back		
For Rheumatoid nodules			Thank the patient		

What determines if the disease is active or not – inflamed or not?
Presence of hotness, tenderness ± rheumatoid nodules

How to differentiate between Acute & Chronic RA?
The presence of joint deformities and muscle wasting indicates chronic disease

What precautions are necessary before upper gastrointestinal endoscopy or general anesthesia in patient with RA?
You must take a cervical spine radiograph to rule out atlanta-axial subluxation.

Differential Diagnosis

SLE, Psoriatic arthritis, Infectious arthritis, Osteoarthritis, Sarcoidosis, Gout.

Treatment

1. Physical rest, and physiotherapy.
2. Drugs

- Anti-inflammatory drugs:
  - Aspirin or NSAIDs.
  - Intra-articular glucocorticoids.
  - Systemic glucocorticoids.
  - These drugs (NSAID and glucocorticoids) control of pain and inflammation, but drugs **do not** alter disease progression.
  - Long term use of NSAID and glucocorticoids can cause peptic ulcer.
- Disease-modifying antirheumatic drugs (**DMARDs**):
  - These agents need to be started early in the course of disease (ideally within 3 months).
  - These agents can stop progression of disease i.e.development of erosions.
  - All of the DMARD take weeks to months to start working.
    - **Methotrexate**: **is first-line drug**, given as weekly low-dose oral or parenterally administered. Remission of rheumatoid arthritis on DMARD therapy has been described in approximately 20 per cent of those with early disease treated with methotrexate or sulphasalazine as single agents.
    - **Sulfasalazine**: is the other first line drug. *Side effects*: GI upset, depression, and reversible oligospermia.
    - **Hydroxychloroquine**: side effect is macular damage, and monitored by eye examination every 6 months to 1 year.
    - **Gold therapy** (either by IM or orally) takes 2-3 months to start acting. *Side effects* include rashes, thrombocytopenia, leukopenia, aplastic anemia and glomerulonephritis (nephrotic syndrome). About 60% of patients may be expected to benefit from gold therapy.
    - **D-penicillamine** can cause nephrotic syndrome.
- **Anti-cytokine therapy**—
  - TNF modulatory agents:
    a. Etanercept: s/c administration, can cause demyelination
    b. Infliximab: IV administration, risks include reactivation of TB
    c. Anti- TNF drugs as DMARD can ↓ disease progression. And are used in pts with inadequate response to at least two DMARDs including methotrexate.
  - IL-1 receptor antagonist (anakinra) can improve the signs & symptoms of RA but it is less effective than anti-TNF drugs.
- Immunosuppressive therapy—**e.g.**, azathioprine, cyclosporine, and cyclophosphamide. Generally reserved for pts who have failed DMARDs.

3. Surgery—may be considered for severe functional impairment due to deformity.

Carpal tunnel syndrome

Definition: Carpal tunnel syndrome is caused by compression of median nerve in the carpal tunnel and is the commonest peripheral nerve entrapment disease.

Epidemiology
Age: most common in middle-aged persons.
Gender: more common in **females**.

History
- The disease is usually bilateral.
- Pain and pins and needles in thumb, index, middle finger which are more at night
- Pain in the forearm may occur

Examination
- Weakness of thumb abduction
- Weakness touching base of little finger
- Wasting of thenar eminence (NOT hypothenar)
- **Tinel's sign**: Tinel's sign is defined as focal pain and electrical sensation elicited by tapping on the median nerve at the wrist.
- **Phalen's test/sign**: maneuver in which the wrist is maintained in flexion by asking the patient to raise both arms opposing the dorsum of the hands; paresthesia occurring in the distribution of the median nerve within 60 sec is indicative of carpal tunnel syndrome.
- **Flick sign**: By asking the patients what they do when their hands and wrist symptoms occur. The response is positive if pts demonstrate flicking motions of hands and wrists-as if shaking thermometer.

Causes
ARMPIT: **A**cromegaly & **A**myloidosis, **R**A, **M**yxedema, **P**regnancy, **I**diopathic, **T**rauma (lunate fracture), and diabetes.
Most common cause is idiopathic

Investigations
Nerve conduction study shows → motor + sensory prolongation of the action potential

Treatment **WRIST**
Wrist splint at night
Rest
Incision decompression (flexor retinaculum division)
Steroid injection
Take diuretics

Raynaud's

Raynaud's may be primary (Raynaud's disease) or secondary (Raynaud's phenomenon) both have similar clinical presentation:

- Episodic color change of fingers ± toes in response to cold.
- The color changes, are White (Ischemia) then Blue (Stasis) then Red (Reactive hyperemia)

Raynaud's disease (idiopathic) typically presents in young women < 30 yrs old and they have no features of an underlying disorder.

Raynaud's phenomenon (Secondary causes) suggested if the pt is male or female > 30 yrs.

- Connective tissue disorders: scleroderma (most common), SLE, Sjögren's, dermatomyositis, and rheumatoid arthritis (least common).
- Leukemia
- Cryoglobulinemia
- Use of vibrating tools
- Drugs: oral contraceptive pill, ergot, β-blockers
- Cervical rib

Management

- Avoid exposure to cold
- Calcium channel blockers (e.g. nifedipine, amlodipine)

Systemic Lupus Erythematosus (SLE)

Definition

SLE is a chronic autoimmune disorder characterized by multisystem involvement and clinical exacerbations and remissions. **Circulating immune complexes** and **autoantibodies** cause tissue damage and organ dysfunction. SLE can affect any organ, but skin, joints, kidneys, brain, serosal surfaces, and blood cells are particularly characteristic.

Epidemiology

Prevalence: 50/100,000 populations. SLE is the most common multisystem CTD
Age: peak age of onset is 15-40 years.
Gender: more in Females. F/M ratio is 10:1.
Race: more in black.
HLA associations: HLA-B8, HLA-DR2 and HLA-DR3
Genetic: concordance rate in identical twins ~50%, but only 2% in siblings.

Clinical manifestations

90% of pts are women, of child-bearing age. The course of disease is characterized by periods of relapse interspersed by periods of remission
Common features include:

- *Constitutional*: fatigue is the most troublesome symptom, fever, weight loss
- *Cutaneous*—rashes (especially malar "butterfly" rash), photosensitivity, livedo reticularis, alopecia, oral ulcers.
- *Arthritis*:
  - Inflammatory, Polyarticular, Symmetric, Migratory.
  - The disease is **Nonerosive = Deformities are rare**, but may occur due to tendon damage and called (**Jaccoud's arthropathy**)
  - Arthralgia is the commonest symptom
  - Arthralgia or arthritis + Raynaud's phenomenon is the most common presentation.
- *Hematologic*—Anemia (may be hemolytic), neutropenia, lymphopenia, thrombocytopenia, lymphadenopathy, splenomegaly, venous or arterial thrombosis.
- *Cardiopulmonary*—pleuritis (most common pulmonary symptom), lung fibrosis, shrinking lung syndrome, pericarditis (most common cardiac symptom), myocarditis, cardiomyopathy, **Libman-Sacks** endocarditis.
- ***Renal involvement in SLE***
  - Glomerulonephritis is the most serious and fatal manifestation of SLE therefore Early diagnosis and treatment are important.
    [illegible]nly nephrotic syndrome, but may present with nephritis.
  - [illegible]ce may be detected by the finding of hematuria and/or proteinuria on routine stick testing of the urine, RBC cast on analysis.
  - [illegible]easurement of BP & urine analysis should be done at each visit.
    [illegible]peritonitis, vasculitis
- *Neurologic*— seizures, psychosis [visual hallucination], cerebritis, peripheral neuropathy, mononeuritis multiplex.

Drug-Induced Lupus

- A clinical and immunologic picture similar to spontaneous SLE may be induced by drugs; in particular:

  1. Procainamide 2.Hydralazine 3.Isoniazid 4.Chlorpromazine 5.Methyldopa 6.Phenytoin 7.Minocycline

- Features are predominantly constitutional, joint, and pleuropericardial; CNS and renal disease are rare.
- Ix: All pts have antinuclear antibodies (ANA); **antihistone antibodies** may be present, but antibodies to dsDNA and low C3&C4 are uncommon.
- Rx: Most pts improve following withdrawal of offending drug.

SLE in pregnancy

- Fertility is not affected by SLE. But there is increased risk of abortion.
- There is no increased risk flare during pregnancy.
- There is a risk of maternal autoantibodies crossing placenta, which leads to condition termed neonatal lupus erythematous.
- Neonatal complications include **congenital heart block**, is associated with **anti-Ro (SSA) antibodies**.

Discoid lupus erythematous

Discoid lupus erythematous is a benign disorder, seen in younger females. It **very rarely progresses to systemic lupus erythematosus**.

Clinical manifestations

- Erythematous, raised or flat rash covered with scales.
- may be photosensitive → more common on face, neck, ears and scalp
- lesions heal with atrophy, scarring (may cause scarring alopecia)

Management

- Topical steroid cream
- **Oral antimalarials** may be used second-line e.g. hydroxychloroquine
- Avoid sun exposure

Investigations

1. **Laboratory:**
   - ESR is ↑ but the **CRP is characteristically normal** [↑ CRP indicate underlying infection]
   - CBD: may show anemia, ↓Plt, ↓WBC.

Immunology:

- Presence of ANA is a cardinal feature (99% of pts are positive), but a (+) ANA is not specific for SLE, and high titers don't correlate with severity.
- Anti-dsDNA: highly specific (> 99%), but less sensitive (70%)
- Anti-Sm: most specific (> 99%), sensitivity (30%)
- Anti-Ro: SLE (50%): **Maternal anti-Ro antibodies associated with neonatal lupus and congenital heart block**
- Rheumatoid factor is positive in 30% of pts.
- VDRL, PT, PTT, anticardiolipin antibody, lupus anticoagulant.
- **Consideration of renal biopsy if evidence of glomerulonephritis**

Monitoring

- Anti-dsDNA titres can be used for disease monitoring

Diagnosis:

Made in the presence of four or more of published criteria.

The criteria contains 11 items, 8 are clinical (4 are dermatological), and 3 laboratory

Diagnostic Criteria for Systemic Lupus Erythematosus		
Clinical	Malar rash	Fixed erythema, flat or raised, over the malar eminences, and the nasolibial fold is spared.
	Discoid rash	Erythematous circular raised patches, covered with scales and atrophic scarring may occur
	Photosensitivity	Exposure to ultraviolet light causes rash
	Oral ulcers	Includes oral and nasopharyngeal ulcers [usually painless]
	Arthritis	Nonerosive arthritis of two or more peripheral joints, with tenderness, swelling, or effusion
	Serositis	Pleuritis or pericarditis documented by ECG or rub
	Renal disorder	Proteinuria >0.5 g/d or ≥ 3+, or RBC casts
	Neurologic	Seizures or psychosis without other causes
Laboratory	Hematologic disorder	Hemolytic anemia or leukopenia (<4000/^{M}L) or lymphopenia (<1500/^{M}L) or thrombocytopenia (<100,000/^{M}L) in the absence of offending drugs
	Immunologic	Anti-dsDNA, anti-Sm, and/or anti-phospholipid
	Antinuclear antibodies	An abnormal titer of ANA, in absence of drugs known to induce ANAs.
If ≥ 4 of these criteria are present at any time in a patient's history, the diagnosis is likely to be SLE.		

Treatment

Education

- Rest when the disease is active.
- Low fat diet in patients with hyperlipidemia.
- Protection from photosensitivity with sun-block.

Drugs

- NSAID: joint disease, serositis, and constitutional symptoms.
- Antimalarial Chloroquine (or Hydroxychloroquine): used in cutaneous, joint, and constitutional manifestations.
- Dapsone is useful for cutaneous manifestation of SLE
- Corticosteroids: used topically for inflammatory rashes, orally for active disease, and IV for acute severe manifestation (CNS lupus or lupus nephritis).
- Azathioprine, methotrexate may be used as steroid sparing agent

- **Cyclophosphamide** suppresses **Lupus nephritis** and reduces the risk of end-stage renal disease. May also benefit hematological and CNS complications. ACEI may help in SLE nephritis.
- Anticoagulation is used in antiphospholipid syndrome. INR (2.5-3.5)

Prognosis

Overall 5 years survival is 90%.

Poor prognosis at time of diagnosis is associated with:

- Nephritis:
  - High serum creatinine levels.
  - Hypertension.
  - Nephrotic syndrome.
- Anemia.
- Hypoalbuminemia.
- Hypocomplementemia.
- Male sex.
- African American.

The main cause of death in SLE are cardiovascular, CNS lupus, infections, and renal failure

Mixed connective tissue disease

Features of SLE, Systemic sclerosis and Polymyositis

Anti-RNP positive

Anti-ribonuclear protein (anti-RNP) = mixed connective tissue disease

Systemic sclerosis

Definition: Systemic sclerosis (Scleroderma) is a condition of unknown etiology characterised by connective tissue fibrosis resulting in hard, sclerotic skin and other connective tissues.

Epidemiology

It is rare disease.
Age of onset around 40 yrs.
Gender: more in **females** ratio (4:1).

Etiology and pathology

- The cause of the disease is not known.
- The Histopathological there is inflammation of skin with infiltration by T lymphocytes and abnormal fibroblast activation producing collagen leading to fibrosis and atrophy.

Clinical presentation

Cutaneous:

Painless edema of the skin followed by fibrosis occurs in many sites:

- Finger become fibrotic and called **Sclerodactyly**.
- Face fibrosis and atrophy in the → **peaked nose**, small mouth **(microstomia)** & telangiectasia.
- Skin may show **(salt-and-pepper)** appearance, with areas of hyperpigmentation alternating with areas hypopigmentation.
- **Raynaud's phenomenon occurs in 95%** of pts, & precede onset of disease.
- Subcutaneous calcification occurs around fingertips and may ulcerate.

Arthralgias and/or arthritis

GI—replacement of esophageal muscle with fibrous tissue results in dysphagia and GERD, & intestinal hypofunction → bacterial overgrowth & malabsorption
Water-melon stomach occur and is associated with upper GIT bleeding
Pulmonary—ILD, pulmonary hypertension.
Renal: hypertension; renal crisis/failure (leading cause of death)

- Renal crisis is characterized by sudden High BP > 160/90 mmHg with rapid deterioration of renal function with proteinuria; and elevated plasma renin activity. If renal crisis is not treated with ACEI it's fatal.

Cardiac—Pericarditis, cardiomyopathy, conduction abnormalities

There are three patterns of disease:

3

1. Limited cutaneous systemic sclerosis

- Raynaud's may be first sign
- Skin involvement limited to face and extremity distal to elbows.
- Associated with Anti-centromere antibodies (sensitivity 60 % specificity 100%)

- Pulmonary hypertension is common.
- Subtype of limited systemic sclerosis is **CREST** syndrome: Calcinosis, Raynaud's phenomenon, Esophageal dysmotility, Sclerodactyly, Telangiectasia
- Good prognosis

2. Diffuse cutaneous systemic sclerosis

- Rapid development of symmetric skin thickening of proximal and distal extremity, face, and trunk.
- Associated with scl-70 antibodies (sensitivity 40 %, specificity 100%).
- Renal involvement is common.
- Poor prognosis

3. Scleroderma (without internal organ involvement) Only skin and it may be:

- Patch and called (**Morphoea**).
- Linear.
- **En coup de saber**: Linear scleroderma occurring on the face or scalp and is often associated with hemiatrophy of the face on the same side.

Investigations

Antibodies

- Anti-scl-70 antibodies associated with diffuse cutaneous SSc.
- Anti-centromere antibodies associated with limited cutaneous SSc.
- ANA positive in 80%
- RF positive in 30%
- Complement levels are normal
- **Skin biopsy** is diagnostic

Treatment

No treatment alters the prognosis except for angiotensin-converting enzyme inhibitors (ACEI) in accelerated hypertension which do preserve renal function.

Symptomatic treatment for various features may help:

- Antibiotics for blind loop syndrome.
- Calcium channel blockers useful for Raynaud's phenomenon.
- Epoprostenol infusion for digital ischemic episode.
- Glucocorticoids , D-Penicillamine are not effective..

Prognosis

The 5-year survival rate is 70 %.

Factors that adversely affect outcome are:

- Increasing age.
- Male.
- Extent of skin involvement.
- Heart, lung, and renal disease.

Sjögren's syndrome

Definition

Sjögren's syndrome (also called sicca syndrome) is an idiopathic, autoimmune disorder affecting exocrine glands resulting in dry mouth **(xerostomia)** and dry eyes **(keratoconjunctivitis sicca)**. Variable lacrimal or salivary gland enlargement can occur (due to lymphocytic infiltration of these glands).

Sjögren's syndrome is classified into:

- **Primary Sjögren's syndrome (PSS)** where the disease exists on its own
- **Secondary Sjögren's syndrome** where it is associated with other diseases. And it usually develops around 10 years after the initial onset. Secondary associations are RA, SLE, scleroderma, polymyositis, & PBC.

Epidemiology

Age of onset 40-60

Gender: more common in **females** (ratio 9:1).

HLA association: HLA-B8/DR3

Clinical manifestations

- Dry eyes due to decreased tear production **(keratoconjunctivitis sicca)**. And they have burning and gritty sensation.
- Dry mouth **(xerostomia)**
- Vaginal dryness
- Arthralgia, myalgia, and Raynaud's phenomena
- Parotid glands enlargement
- Other: Lymphadenopathy, Sensory polyneuropathy, ILD, RTA.

Investigation

- Schirmer's test: flow of tears over 5 minutes using absorbent paper strips placed in the lower lachrymal sac; a normal result is greater than 6 mm of wetting. Positive Schirmer's test indicates dry eyes.
- Saxon test, an oral equivalent of the Schirmer test, when positive it indicates dry mouth.
- Antibodies:
  - **Anti-Ro (SSA)** antibodies in 70% of pts with PSS. **Anti-La (SSB)** antibodies in 30% of pts with PSS, if both are +ve it is specific for Sjögren's syndrome.
  - Rheumatoid factor (RF) positive in 90%, ANA positive in 70%.
- Lip or salivary gland biopsy is the most definitive diagnostic test & shows focal lymphocytic infiltration. They are done when antibody tests are -ve.

Management

- Artificial saliva and tears
- Pilocarpine may stimulate saliva production

Prognosis: There is a marked increased risk of **lymphoma** (40-60 fold)

Dermatomyositis & Polymyositis

Overview

- Dermatomyositis is an inflammatory disorder causing symmetrical, proximal muscle weakness and characteristic skin lesions
- Polymyositis is a variant of the disease where skin manifestations are not prominent.
- Both may be idiopathic or **in adults** is associated with connective tissue disorders or **underlying malignancy** (found in 30 %)
- The peak incidence occurs from 40 to 60 year, more in females.

Clinical features

Skin features which occurs in Dermatomyositis but not Polymyositis

- Photosensitive
- Erythematous rash over anterior chest (**V sign**), and shoulder (**shawl sign**)
- **Heliotrope rash** over cheek and eyelids
- **Gottron's papules** (pathognomonic) - rough red papules over the knuckles of fingers
- Calcinosis cutis (deposition of calcium in the skin), in children > adults

Other features which occur in both Dermatomyositis and Polymyositis

- Systemic features of fever, weight loss and fatigue are common.
- Subacute onset proximal muscle weakness in arms and legs causing difficulty with rising from a chair, sitting up in bed, or combing hair.
- Muscle pain and tenderness are not typical.
- Respiratory muscle weakness due to involvement of the diaphragm, Dysphagia due to involvement of esophagus.
- Cardiac muscle involvement is uncommon & results in cardiomyopathy
- Raynaud's phenomena
- Interstitial lung disease

Investigations

- Elevated creatine kinase (CK) is raised in > 70% of cases, Lactic dehydrogenase (LDH) is also elevated, and both are used pt follow up.
- EMG is abnormal in almost all cases, and it confirms the diagnosis and excludes peripheral neuropathy as a cause.
- Muscle biopsy is needed in most of cases.
- antisynthetase (anti-Jo-1) antibodies are common in polymyositis
- ANA positive in 60%

Management

- Treatment should be started quickly, because delay is associated with poorer outcome.
- High-dose prednisolone is the drug of choice 85% of pts respond, and in those who don't respond methotrexate or azathioprine are started.
- Intravenous immunoglobulins can be useful

Seronegative spondyloarthropathies

Spondyloarthropathies
- Ankylosing spondylitis
- Psoriatic arthritis
- Reiter's syndrome (including reactive arthritis)
- Enteropathic arthritis (associated with IBD)

Spondyl means vertebra.

Seronegative, refers to the absence of rheumatoid factors in these diseases.

ALL seronegative spondyloarthropathies share the following features:
- **Associated with HLA-B27**.
- **Rheumatoid factor negative.**
- **Asymmetrical inflammatory oligoarthritis** [More in lower limbs]
- **Sacroilitis**
- The main abnormity is at insertion of tendons & ligaments (**enthesitis**) NOT the synovium. E.g. Achilles tendonitis, plantar fasciitis.
- Extra-articular manifestations: uveitis, pulmonary fibrosis (upper zone), amyloidosis, aortic regurgitation, Erythema nodosum

Psoriatic arthropathy

Psoriatic arthropathy correlates poorly with cutaneous psoriasis and often precedes the development of skin lesions.

Epidemiology
- Around 10% of pts with psoriasis develop an arthropathy
- Males = Females.
- There is no correlation between severity of skin disease & joint disease.

Types
- Asymmetrical oligoarthritis: characteristically fingers or toes become inflamed → Sausage digit or dactylitis
- Sacroilitis
- Rheumatoid-like polyarthritis
- **DIP joint disease**
- **Arthritis mutilans** (severe deformity fingers → **telescoping fingers**)

X-ray: marginal erosions, with ↑ sclerosis of small bones (**ivory phalanx**).

Management
- Treat as rheumatoid arthritis, but these pt have better prognosis

Ankylosing spondylitis

Overview

- The main pathological changes here are enthesitis of the **sacroiliac** and **spine joints** (intervertebral discs) and this enthesitis heals with fibrosis and **calcification** of these joints → fusion of vertebrae = ankylosing spondylitis.

Epidemiology

Age: 20-30 years old

Gender: more in **males** (sex ratio 3:1)

HLA association: HLA-B27

- HLA-B27 is not useful in making diagnosis as it is positive in 95% of patients with ankylosing spondylitis, and 10% of normal patients.

Clinical manifestations

- Typically a young man who presents with lower back pain and stiffness
- Stiffness is usually worse in morning and improves with activity, and there is tenderness over the affected joints.
- It starts in lumbar area & then ascend to affect thoracic and cervical spine and it leads to:
  - Loss Lumbar lordosis
  - Decrease chest expansion at thoracic spines due to ankylosis costovertebral joints.
  - Kyphosis of cervical spine s
- Calcification of vertebrae may → narrowing of spinal canal → Cauda equina syndrome
- Peripheral oligoarthritis mainly affect the knee and hip
- Plantar fasciitis & Achilles tendonitis

Extraarticular manifestations

Eye: Anterior uveitis and conjunctivitis

Pulmonary: **Apical lung fibrosis**

Cardiovascular:

- **Aortic regurgitation**
- Mitral regurgitation
- AV node block
- Pericarditis

Others:

- Amyloidosis (nephrotic syndrome, and peripheral neuropathy)
- Prostatitis

Examination

Shober test: it is a test for spinal flexion. Two points on the patient's lumbar spine the lumbar sacral junction and a point 10 cm above are marked while the patient is standing. Then the distance is remeasured after the patient bends to touch the toes. (An elongation < 5 cm suggests spine stiffness).

Investigations

- Hematology: ↑ESR & CRP in active disease, anemia (normocytic, normochromic)
- Biochemistry: features of nephrotic syndrome (amyloidosis)
- Radiology:
  - X-ray of the sacro-iliac joints is the most useful investigation for establishing diagnosis and monitoring disease.
    X-rays are often early in the disease, later changes include:
    - Sacroilitis: subchondral erosions, sclerosis
    - **Squaring** of lumbar vertebrae
    - **Bamboo spine**
  - Chest x-ray: apical fibrosis.
- Spirometry may show a restrictive defect due to a combination of pulmonary fibrosis, kyphosis and ankylosis of the costovertebral joints

Management

- Continued activity and Physiotherapy. *(Long periods of bed rest are avoided as much as possible)*
- NSAIDs relieve symptoms of pain but no effect on the course of disease.
- DAMARD. Sulphasalazine and methotrexate are useful in peripheral joint involvement – but don't improve spinal mobility.
- Anti-TNF-alpha is useful in both peripheral and axial joint diseases.

Prognosis

- Most pts have good prognosis.

Enteropathic arthropathy

Definition: enteropathic arthropathy is defined as arthritis associated with inflammatory bowel disease.

Clinical presentation: Both sacroilitis and peripheral arthritis (affecting weight bearing joints occur).
Peripheral arthritis correlates with disease activity
Sacroilitis does not correlate with disease activity

In patients with ulcerative colitis, the peripheral arthritis occurs at time of flares, & in patients with severe disease &pan-colectomy cures the arthropathy.
In Crohn's also peripheral arthritis correlates with disease activity.
In both UC and CD sacroilitis doesn't follow the course of the disease.

Reactive arthritis

Definition: a inflammatory arthritis strongly related to a recognized episode of infection with **no** viable microorganism in the affected joints. Reactive arthritis includes **Reiter's syndrome**, a triad of **urethritis**, **conjunctivitis** and **arthritis**.

Epidemiology

- Common in young **men** (ratio 15:1) and is the most common cause of inflammatory arthritis in men < 35 years.

Etiology

Organisms often responsible for post-dysenteric form

- Shigella flexneri
- *Salmonella* typhimurium
- *Yersinia enterocolitica*

Organisms often responsible for post-STI form

- Chlamydia trachomatis

Clinical manifestations

- Typically develops 2-4weeks after infection - symptoms generally last for 2-4 months
- Arthritis is an inflammatory asymmetrical oligoarthritis of lower limbs.
- Pt may present as enthesitis Achilles tendonitis, plantar fasciitis
- Symptoms of urethritis – dysuria
- Eye: conjunctivitis, anterior uveitis
- Skin:
  - **Circinate balanitis** (painless vesicles on the coronal margin of the prepuce and glans of the penis)
  - **Keratoderma blenorrhagica** (waxy yellow papules on palms & soles)
  - Buccal erosions (painless)

25% of pts have recurrent episodes and 10% of pts develop chronic disease

Management

- NSAID

Gout

Definition: Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricemia (uric acid > 450 μmol/l).

Epidemiology

- More common in **males** aged 40-50 **years**.
- Gout almost never occurs in premenopausal females.

Etiology and pathophysiology

- Uric acid is produced by the breakdown of purine bases. The enzyme responsible for this is xanthine oxidase. Uric acid is excreted in the kidney.
- Decreased renal excretion of uric acid is the cause gout.
- Monosodium urate (MSU) crystals present in the joint are phagocytosed by leukocytes → release of inflammatory mediators → synovial inflammation.

Predisposing factors

Decreased excretion of uric acid

- Drugs: Diuretics (Thiazides, Frusemide), low dose Aspirin, Pyrazinamide
- Alcohol
- Renal failure

Increased production of uric acid

- Dietary intake of purine
- Myeloproliferative/lymphoproliferative disorder
- Cytotoxic drugs

Clinical Manifestations

- ***Acute inflammatory arthritis***:
  - Extremely painful **monoarthritis** and the involved joint is erythematous, swollen, and warm.
  - ***Podagra*** (attack in the great toe) i.e. first metatarsophalangeal joint, it is the site of first attack in 50% of pts & will occur in 90% of pts.
  - Attack subsides in 5-14 days. With pruritis & desquamation of overlying skin are common.

Differential diagnosis: septic arthritis, pseudogout.

- ***Chronic tophaceous gout***: aggregates of MSU crystals form white nodules called (**tophi**) deposit at extensor surfaces of fingers, elbows, Achilles tendons & pinna of the ear. Large nodules may ulcerate → discharge white material looking like pus.

Kidney

- → ***Acute uric acid nephropathy***—reversible cause of ARF due to precipitation of urate in the tubules.
- → ***Urate nephrosis***—deposition of MSU crystals in interstitium and pyramids. Can cause CRF.
- → ***Uric acid stones***

Investigations

• CBC → leukocytosis. • ESR and CRP are ↑.

•**Joint aspiration [Synovial fluid analysis]:** the only definitive investigation. It is characteristic by: needle-shaped negatively birefringent MSU crystals by polarizing microscopy.

• **Serum uric acid**—normal levels do not rule out gout. Uric acid levels may be normal in 20% of acute attacks.

• Joint x-rays: may → **punched out** cortical erosions (away from the margin)

Management

➢ **Acute management**

1. NSAIDs is the Rx of choice.
2. Colchicine (inhibitor of neutrophil microtubular assembly) has slow onset of action. SE: diarrhea.
3. Therapeutic joint aspiration
4. Intra-articular steroid injection

- Allopurinol **should not** be started until 2 weeks after remission of the acute attack, because initiation of Allopurinol may prolong the attack. But if the pt is already taking allopurinol it should be continued

➢ **Long term management**

1. ↓ Protein intake, ↓ Wt if obese, ↓ Alcohol, ↓ Diuretics
2. **Allopurinol prophylaxis**
   - Allopurinol is a **xanthine oxidase** inhibitor.
   - NSAID or colchicine cover is used when starting allopurinol.
   - Indications for allopurinol:
     1. Recurrent attacks
     2. Tophi (treatment can dissolve tophi)
     3. Renal disease or Uric acid renal stones
     4. Bone or joint damage
     5. Gout with greatly elevated serum uric acid
     6. Prophylaxis if on cytotoxics or diuretics

Note: Asymptomatic hyperuricemia should not be treated.

Pseudogout

Definition: Pseudogout is a synovitis caused by the deposition of **calcium pyrophosphate dihydrate** (CPPD) crystals in the synovium.

Epidemiology

- Pseudogout is the most common cause of acute monoarthritis in elderly.
- **Age: 65 to 75** yrs
- **Gender**: more in **female**.

Clinical presentation

- ***Acute pseudogout:*** it presents with monoarthritis with **knee is most commonly involved joint**. wrist and shoulders may be affected.
- ***Chronic arthropathy***- -progressive degenerative changes in multiple joints. Common sites including knee, wrist, 2nd and 3rd MCP, hips, and shoulders.

Investigation

- Aspiration of joint fluid, to exclude septic arthritis and show weakly-positively birefringent brick shaped crystals.
- X-ray: **(chondrocalcinosis)** calcification in hyaline cartilage and/or fibrocartilage [knee menisci, triangular cartilage of the wrist].

Management

- Acute pseudogout: as acute gout
  - Joint aspiration
  - Intra-articular corticosteroid
  - NSAIDs and colchicine
- Chronic arthropathy: as OA

Septic arthritis [ER]

Definition: Acute inflammatory condition of a joint due to bacterial infection.

Epidemiology:
- The most rapidly destructive joint disease → permanent damage
- Risk factors → DM
  → Pre-existing joint disease (RA)

Age: more in children

Etiology:
- **Staph. aureus** (the most common cause)
- Neisseria gonorrhea [H/O STD + skin lesions]
- Salmonella in pts with sickle cell anemia
- Other [H. influenza, streptococci]

Organism enter joint by → Hematogenous spread (most common)
→ Penetrating wound

Clinical picture
- Acute inflame. **monoarthritis** which is severely painful, hot, & red.
- knee is the commonest joint affected [except in < 1yr hip is most common]

Investigations
- CBC→ leukocytosis. ESR ↑ & CRP ↑
- **Joint aspiration** with Synovial fluid for Gram stain & culture.
  Synovial fluid looks turbid or blood-stained.
- Blood cultures.
- X-ray

Treatment
- NSAID for pain
- Drainage of the joint
- IV Empirical Antibiotics (e.g. flucloxacillin) for 6 weeks

Vasculitis

Definition

- Vasculitic syndromes are a group of disorders characterized by inflam. of bl. vessels → damage + narrowing of bl. vessel lumen → ischemia.
- Vasculitis can be a primary or as a secondary manifestation of infectious, malignant, or rheumatic disease.
-

Classification of vasculitis according to the size of bl. vessel affected

Large → Temporal arteritis
Large → Takayasu's arteritis
Medium → Polyarteritis nodosa
Small → Wegner's granulomatosis
Small → Churg-Strauss syndrome
Small → SLE

Syndrome	Clinical picture	Pathology	Dx	Rx
Wegener's granulomatosis	•URT (saddle nose, sinusitis, septal perforation) •LRT (cough, hemoptysis, dyspnea) • Renal involvement glomerulonephritis	Necrotizing granulomas	c-ANCA CXR: multiple cavities Lung biopsy	Corticosteroids ± cyclophosphamide
Polyarteritis nodosa	•Nodules on skin •Renal involvement → HTN •Peripheral nerves → palsies •Lungs & spleen spared • Asso. with **hepatitis B.**	Necrotizing arteritis	p-ANCA Biopsy Angiography shows aneurysms	
Churg-Strauss Syndrome	Asthma + eosinophilia + vasculitis	Granulomas + eosinophils	Lung biopsy	
Takayasu's disease (Pulsless disease)	Aorta dis → claudication Young Asian female	Giant cells	Angiography Chest MRI	
Mixed essential cr. globulinemia	Raynaud's phenomona. Associated with **hepatitis C**			

Behcet's syndrome (one of type of vasculitis)

Definition: multisystemic dis. due to autoimmune inflame. of arteries & veins

Etiology: unknown

Epidemiology

- More common in **eastern Mediterranean** (e.g. Turkey) - سوريا - لبنان
- **Age**: young (20 - 40 yrs)
- **Gender**: more in **males**.
- HLA associations: **HLA B51**

Clinical presentation :

Classical triad
- **Oral ulcers** must be found > for Dx pt
- **Genital ulcers**
- **Anterior uveitis**

- Ulcers are painful
- **Eyes disease is the most serious complication of Behcet's disease**
  - Most common eye problem is **uveitis ± hypopyon** (sterile) → collection of pus in Ant. Chamber
  - Other eye features are episcleritis, scleritis, retinal vasculitis, iridocyclitis, chorioretinitis, optic atrophy, conjunctivitis & keratitis.
  - [**25% of patients with ocular involvement become blind**]
- **Skin: Erythema nodosum**, pseudofolliculitis, papulopustular lesions
- Vascular: Thrombophlebitis, DVT, aneurysm (abdominal aorta, pulmonary artery). pulmonary embolism is poor prognostic factor
- Arthritis: non-destructive commonly affects knees, ankles, and elbows.
- Neurological involvement (e.g. aseptic meningitis, meningoencephalitis) ↓ level of consciousness
- GIT: abdominal pain, diarrhea, colitis

Diagnosis

- **No definitive test** and diagnosis is based on clinical criteria

Criteria to Dx Behcet's disease
• **Recurrent oral ulceration** + Any 2 of the following:
1. Recurrent genital ulceration
2. Eye lesions
3. Skin lesions
4. Positive **pathergy test** [pustule forms at site of needle puncture]

Treatment

- Corticosteroids. (skin/mucosal lesions), It has no effect on eye involvement
- Colchicine (skin/mucosal lesions)
- Thalidomide (skin/mucosal lesions) methotrexate
- Immunosuppressive drugs (azathioprine, Cyclosporin A) are the main line of treatment for eye involvement.

Poor Prognostic features
- Young **males** have the worst prognosis
- Pulmonary artery aneurysm.

Giant cell arteritis & Polymyalgia rheumatica

Giant cell arteritis is a large vessel vasculitis mainly affecting the temporal and ophthalmic arteries.
There is an overlaps between Giant cell arteritis & Polymyalgia rheumatica

Epidemiology → Age: > 60 years old
→ Gender: more in females

Clinical presentations

- Severe headache
- Jaw claudication: which is pain on talking or chewing
- Tender, palpable temporal artery, which is thick and non-pulsatile
- Sometime the first presentation is monocular blindness
- Other: lethargy, depression, low-grade fever, anorexia, night sweats

If the pt has **morning stiffness** in proximal limb muscles (not weakness, or wasting) the condition is called [Polymyalgia rheumatica]

Investigations

- ↑CRP and ↑ ESR > 50 mm/hrs
- Temporal artery biopsy: **skip lesions** [some sections are affected while other sections are normal → negative result does not exclude the Dx]
- **CK and EMG normal**

Treatment

- High-dose prednisolone (dramatic response)
- Treatment should be started immediately to ↓ the chance of visual loss

Fibromyalgia

Definition: a clinical syndrome, characterized by chronic, generalized pain in joints, muscles, and the spine. But there is no arthritis.
Etiology: unknown
Epidemiology → **Age**: middle age
→ Gender: **female**
Clinical picture

- Sever Fatigue more in the morning + Multiple tender points in palpation affecting the muscles of neck, back, and over bony prominances.
- Pts usually have associated → Depression
  → Sleep disturbance
  → Irritable bowel syndrome

Investigations: it is the diagnosis of exclusion [ALL investigations are normal]
Treatment

- Reassurance
- Cognitive-behavioral therapy
- Tricyclic antidepressants [e.g. Amitriptyline]

Note: NSAIDS are not effective

Osteoarthritis

Definition. Osteoarthritis (OA), also called degenerative joint disease, is a disorder characterized by progressive deterioration and loss of articular cartilage accompanied by proliferation of new bones in & around joint

Epidemiology

- **OA is the most common form of joint disease.**
- **Age**: old age-> 60 years.
- **Gender:** More in females.
- **Race:** More in white.
- Other risk factors: joint trauma, prior inflame. disease (RA), Hemochromatosis, Acromegaly

Clinical Manifestations

- OA can affect any joint, but mostly monoarticular, in weight-bearing and frequently used joints such as the knee, hip, spine, and hands.
- The hand joints that are typically affected are the DIP, PIP, first carpometacarpal (thumb base); MCP joint involvement is rare.
  - **Pain** is the is the commonest symptom
  - **Stiffness** after rest or in morning may occur but usually brief (< 30 min)
  - **Crepitation** ("crackling")
  - **Joint** deformity:
    - **Bouchard's nodes:** bony enlargements of PIP joints.
    - **Heberden's nodes:** bony enlargements of DIP joints.

Classical radiographic findings of OA:

- Stage1- Joint space narrowing (most important sign)
- Stage2- New bone formation (**osteophyte**)
- Stage3- Subchondral bone sclerosis
- Stage4- Subchondral cyst formation and trabecular fracture.
- In OA there is no osteoporosis around the affected joint.

Management

- Advice to ↓ Weight, & give advice strengthen local muscles.
- Paracetamol and topical NSAIDs are first-line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand.
- Second-line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream and intra-articular corticosteroids.
- Non-pharmacological treatment options include supports and braces.
- If conservative methods fail → consideration of joint replacement